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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/036,129 | 12/26/2001 | Rajneesh Tancja | ABB1259P0072US (6762.US.0 | 3432 |

7590 05/02/2006

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| EXAMINER | |
|---|---|
| SHEIKH, HUMERA N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | |

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/036,129 | TANEJA ET AL. | |
| | Examiner | Art Unit | |
| | Humera N. Sheikh | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,9-21 and 23-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-21 and 23-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Humera N. Sheikh
PATENT EXAMINER
TC-1600

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/09/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### Status of the Application

Receipt of the Request for Continued Examination (RCE) under 37 C.F.R. 1.114, the Amendment, Applicant's Arguments/Remarks and the Information Disclosure Statement (IDS), all filed 02/09/06 is acknowledged.

Applicant has overcome the following objection(s) and/or rejection(s) by virtue of the Amendment and/or Remarks:

(1) The New Matter objection for claims 1, 15 and 26 has been withdrawn.

(2) The 35 U.S.C. §112, second paragraph rejection for claims 1 and 2 has been withdrawn.

(3) The 35 U.S.C. §102(e) rejection of claims 1-7, 9-11, 15-21, 23, 24 and 26-28 over Phillips I ('346) has been withdrawn.

Claims 1-7, 9-21 and 23-33 are pending in this action. Claims 1 and 15 have been amended. New claims 30-33 have been added. Claims 8 and 22 have previously been cancelled. Claims 1-7, 9-21 and 23-33 are rejected.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/09/06 has been entered.

***Inventorship***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant invention is drawn to a method for treating gastric acid disorders comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of at least one non-enteric coating proton pump inhibitor in a pharmaceutically acceptable carrier; wherein said pharmaceutically acceptable carrier comprises an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal where the Group IA metal is chosen from the Periodic Table of Elements.

**Claims 1-7, 9-21 and 23-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US Pat. No. 6,489,346 B1) (hereafter 'Phillips I').**

**Phillips I ('346)** teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

At column 13, lines 47-53, Phillips teach that mixtures of the buffering agents can be utilized. Suitable buffering agents disclosed include sodium bicarbonate, potassium bicarbonate, aluminum hydroxide/sodium bicarbonate co-precipitate and sodium carbonate (see col. 13, line 63 – col. 14, line 14); (col. 17, lines 58-60). Potassium carbonate is disclosed at column 22, lines 7-8. Sodium bicarbonate is provided in amounts of about 1000 mg to about 1680 mg (see claim 17). This amount range is an overlapping range, which meets the instantly claimed range of about 125 mg to about 1000 mg of sodium bicarbonate.

The non-enteric proton pump inhibitors include a substituted benzimidazole of lansoprazole or salts thereof (see Abstract). Example IV at column 22, lines 1-39 demonstrates an effervescent formulation whereby omeprazole powder was diluted with sodium bicarbonate, citric acid and potassium carbonate to form a homogeneous mixture of omeprazole powder.

With regards to the instant amounts, such as the 'equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal' and an 'equimolar ratio of sodium bicarbonate and sodium carbonate', Phillips does not explicitly teach 'equimolar ratios of a bicarbonate and carbonate salt of Group IA metals. However, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In this instance, prior art teaches the use of the same drug (PPI) and the same components (buffer – (bi)carbonates, carrier) in similar dosage forms (tablets, capsules) to effectively treat conditions of gastric acid disorders in a subject in need thereof. Furthermore, it is deemed obvious to one of ordinary skill in the art to determine suitable or effective amounts through the use of routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art. Absent evidence to the contrary, the instant 'equimolar ratios' as claimed fail to impart any unexpected results. The prior art addresses the concern of avoiding large amounts of bicarbonate or other buffers, to overcome any adverse effects (*i.e.*, frequent belching) by administering a single dose,

which does not require any further administration of a bicarbonate (see col. 9, line 28 – col. 10, line 14); (col. 13, lines 7-27).

Thus, given the teachings of Phillips ('346) who teaches a method for treating gastric disorders by administering carbonates and bicarbonates in combination with proton pump inhibitors, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

**Claims 1-7, 9-21 and 23-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US Pat. No. 5,840,737) (hereafter 'Phillips II') in view of Phillips (US Pat. No. 6,489,346 B1) (Phillips I).**

The instant invention is drawn to a method for treating gastric acid disorders comprising the step of administering to a patient in need of such treatment a therapeutically effective amount of at least one non-enteric coating proton pump inhibitor in a pharmaceutically acceptable carrier; wherein said pharmaceutically acceptable carrier comprises an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal where the Group IA metal is chosen from the Periodic Table of Elements.

**Phillips II ('737)** teaches a method for treating gastric acid disorders by administering to a patient a single dose of a pharmaceutical composition including an aqueous solution/suspension of proton pump inhibitors – omeprazole, lansoprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal (see abstract and claims). Phillips also

teaches a pharmaceutical composition, which includes omeprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal (see abstract and claims).

Phillips II teaches a method for treating gastric acid disorders wherein the Group IA metal is sodium and potassium (see claims 1-3).

It is stated that the pharmaceutical composition is prepared by mixing omeprazole or other substituted benzimidazoles and derivatives thereof with a solution including a bicarbonate salt of a Group IA metal. Preferably, omeprazole powder or granules are mixed with a sodium bicarbonate solution to achieve a desired final omeprazole concentration (col. 7, line 50 through col. 8, line 5).

Phillip II states that the pharmaceutically acceptable carrier includes the bicarbonate salt of the Group IA metal and can be prepared by mixing the bicarbonate salt of the Group IA metal, which is preferably sodium bicarbonate, with water. The concentration of the bicarbonate salt of the Group IA metal in the composition generally ranges from approximately 5.0% to about 60%. In a preferred embodiment, the preferred salt is sodium bicarbonate and is contained in a concentration of about 8.4% (col. 8, lines 6-17).

Suitable derivatives of omeprazole can be substituted for the omeprazole or other suitable substituted benzimidazoles, wherein these derivatives include lansoprazole (col. 8, lines 41-45).

The pharmaceutical composition can be used for the treatment of gastrointestinal conditions, including, active duodenal ulcers, gastric ulcers, gastroesophageal reflux disease (GERD), severe erosive esophagitis, poorly responsive systematic GERD, and pathological hypersecretory conditions (col. 8, lines 46-61).

The examples on columns 10-19 further demonstrate various embodiments of the invention in greater detail.

Additional agents that can be added include antimicrobial preservatives, antioxidants, chelating agents and buffers (column 9, lines 23-26).

While Phillips II does not explicitly teach the instant amounts, such as the 'equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal' and an 'equimolar ratio of sodium bicarbonate and sodium carbonate', the Examiner points out that generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicants have not demonstrated any unusual/unexpected results that accrue from the instant equimolar ratios. It is deemed obvious to one of ordinary skill in the art that suitable ratios and/or amounts could be determined through the use of routine or manipulative experimentation to obtain the best possible results, as these are indeed variable parameters obtainable within the art. The prior art vividly recognizes the need to administer lower amounts of bicarbonate to avoid adverse effects in gastroesophageal patients. Thus, the Phillips II reference meets the same objectives desired by Applicants.

Regarding the 'non-enteric' proton pump inhibitor claimed by Applicant, Phillips II teaches a method for treating gastric acid disorders whereby the use of enteric coatings can be used if desired, indicating that enteric coatings are optional. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to either employ

enteric coatings if drug delivery in the intestines was desired or alternatively, to exclude enteric coatings if delivery of drug to the stomach was desired. The expected result would be a drug formulation having distinct rates of release.

Phillips II ('737) does not teach a *carbonate* salt of the Group IA metal.

**Phillips I ('346)** teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a *carbonate salt of a Group IA metal,* whereby suitable buffering agents include sodium carbonate, for example (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the carbonate salt of the Group IA metal of Phillips I ('346) within the teachings of Phillips II ('737) who teaches bicarbonate salts of the Group IA metal because Phillips I explicitly teaches a proton pump inhibitor formulation comprising suitable buffering agents of both carbonates and bicarbonates of Group IA metals and teaches that the buffering agents (*i.e.*, carbonates/bicarbonates) function to substantially prevent or inhibit acid degradation of the proton pump inhibitor by elevating pH of the stomach sufficiently to achieve adequate bioavailability of the drug to effect therapeutic action. The expected result would be a non-enteric coated formulation wherein the bioavailability of the proton pump inhibitor is

preserved to provide for the effective treatment and/or prevention of gastric acid related disorders.

***Response to Arguments***

Applicant's arguments filed 02/09/06 have been fully considered.

Firstly, Applicant argued regarding the New Matter objection to claims 1, 15 & 26 stating, "The Office Action objected to claims 1, 15 & 26 as containing new matter on the grounds that there is no support for an equimolar ratio of a salt of a Group IA metal other than a carbonate or a bicarbonate salt. The term "bicarbonate" was inadvertently omitted from claim 1 in the previous Amendment. The term has been reinserted. Accordingly, this objection should no longer apply."

Applicant's remarks were found persuasive by virtue of the Amendment reinserting the term "bicarbonate' in claim 1. Accordingly, the New Matter objection to claims 1, 15 & 26 has been withdrawn.

Secondly, Applicant argued regarding the 35 U.S.C. 112, second paragraph rejection of claims 1 & 2 stating, "This correction of claim 1 should also address the Section 112 rejection of claims 1 and 2, which should also be withdrawn."

Applicant's remarks were found persuasive by virtue of the Amendment to claim 1. Accordingly, the 35 U.S.C. 112, second paragraph rejection of claims 1 & 2 has been withdrawn.

Thirdly, Applicant argued regarding the 35 U.S.C. 102(e) rejection of claims 1-7, 9-11, 15-21, 23, 24 and 26-28 over Phillips I ('346) stating, "Phillips I discloses a composition comprising a non-enteric coated proton pump inhibitor and at least one buffering agent. While

Phillips I does broadly state that mixtures of buffering agents can be used, there is no disclosure of any specific mixtures. Phillips I does not disclose an equimolar ratio of a carbonate salt and a bicarbonate salt as is presently claimed."

These arguments have been thoroughly considered and were found to be persuasive. Accordingly, the 35 U.S.C. §102(e) rejection of claims 1-7, 9-11, 15-21, 23, 24 and 26-28 over Phillips I ('346) has been withdrawn.

The instant claims have now been rejected under 35 U.S.C. §103(a) over Phillips I ('346). The prior art (Phillips I or '346) teaches compositions and methods for treating gastric acid disorders by the administration of a pharmaceutical composition comprising non-enterically coated proton pump inhibitors (i.e., omeprazole, lansoprazole, other substituted benzimidazoles) and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises bicarbonate salts and carbonate salts of a Group IA metal (see abstract and col. 13, line 47 – col. 14, line 26). The pharmaceutical composition can be used for the treatment of gastrointestinal conditions, including gastroesophageal reflux disease (GERD). As admitted by Applicant, mixtures of buffering agents are disclosed. Applicant's argument that 'no specific mixtures are disclosed' is not persuasive since suitable and preferred buffering agents include bicarbonates, such as sodium bicarbonate as well as carbonates, such as sodium carbonate (see col. 13, line 65 and col. 14, line 5). The mere disclosure of the desire to incorporate mixtures of these buffering agents, as taught by the prior art, would clearly provide for sufficient specification, the particular carbonates and bicarbonates of the Group IA metal as claimed by Applicant. The prior art discloses the same composition comprising a combination of the same active ingredients, used for the same field of endeavor and to treat the same problems as that desired by Applicant.

Applicant's argument that 'Phillips I does not disclose an equimolar ratio of a carbonate salt and a bicarbonate salt as is presently claimed' is not persuasive since Applicants have not demonstrated any superior results attributable to the claimed 'equimolar ratio' amount. The prior art vividly recognizes and teaches similar proton pump inhibiting formulations comprising the incorporation of suitable carriers and buffers to effectively treat acid-related gastrointestinal disorders.

Lastly, Applicant argued with respect to the Section 103(a) rejection stating, "Neither Phillips I ('346) nor Phillips II recognizes the problem addressed by the present invention. High doses of sodium bicarbonate produce large amounts of $CO_2$ and lead to belching which in patients with GERD can worsen their condition. Furthermore, bicarbonates having lower acid-neutralizing capacity than carbonates permitting the use of lesser amounts of buffer and the formation of smaller pills or tablets."

Applicant's arguments have been considered, but were not found persuasive. The prior art clearly teaches a composition comprising carbonates/bicarbonates useful for treating conditions of GERD, as also similarly desired by Applicant. Moreover, it is deemed obvious to one of ordinary skill in the art to determine suitable and effective doses of sodium bicarbonate, which do not cause detrimental side effects to the patient, through the use of routine experimentation to obtain the best possible results. The prior art teaches a proton pump inhibiting formulation comprising the use of the same ingredients for the effective treatment of gastric acid related disorders. Applicant has not demonstrated any surprising and/or unexpected results, which accrue from the instant formulation, nor have any unexpected results been demonstrated through the instant 'equimolar ratio of a bicarbonate salt and a carbonate salt',

since the prior art initially teaches a composition, composed of the same components (*i.e.*, carbonates & bicarbonates salts of a Group IA metal), for use in the same field of endeavor, which would therefore impart the same results as also achieved by Applicant. Additionally, the composition of the prior art is also directed particularly and especially for the treatment of gastroesophageal diseases, as also claimed by Applicant herein. Thus, it is the position of the Examiner, that given the explicit teachings of the prior art, the instant invention, when taken as a whole, would have been *prima facie* obviousness to one of ordinary skill in the art at the time the invention was made.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh Humera N. Sheikh TC-1600

Patent Examiner

Art Unit 1615

April 27, 2006

*hns*